

LISTING OF CLAIMS

Claim 1 (*currently amended*): A method of killing melanoma cells comprising contacting said cells for an effective time with an effective amount of an organic small molecule inhibitor of MAPK/ERK kinase (MEK) enzymes which inhibitor

(i) is a direct, noncompetitive inhibitor of MEK which does not inhibit the binding of the enzyme to one of its substrates, adenosine triphosphate (ATP); and

(ii) induces apoptosis in said cells, thereby killing the cells.

Claim 2. (withdrawn) The method of claim 1, wherein said inhibitor is a MEK-directed protease.

Claim 3. (withdrawn) The method of claim 2, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

Claim 4 (*previously amended*): The method of claim 1 wherein said inhibitor is selected from the group consisting of PD98059, U0126 and PD184352.

Claim 5 (*previously amended*): The method of claim 4 wherein said inhibitor is PD184352.

Claim 6 (*previously amended*): The method of any of claims 1, 4 or 5, wherein said contacting is *in vivo*.

Claim 7 (original): The method of claim 6 wherein said killing results in measurable regression of melanoma tumor or attenuation of melanoma growth.

Claim 8. (withdrawn) A method of protecting against melanoma in a susceptible subject, comprising administering to said subject that is

(a) at risk for development of melanoma or,

(b) in the case of an already treated subject, at risk for recurrence of melanoma,

an effective amount of a MAPK-inhibitor.

Claim 9 (*currently amended*): A method of inducing an antitumor response in a mammal having melanoma, comprising administering an effective amount of an organic small molecule inhibitor of MEK enzyme to said mammal, which inhibitor

(a) is a direct, noncompetitive inhibitor of MEK which does not inhibit the binding of the enzyme to one of its substrates, ATP; and

(b) induces apoptosis in and is cytotoxic to melanoma cells in said mammal, thereby inducing an antitumor response that comprises

- (i) at least a 50% decrease in tumor size measured as the sum of the products of maximal perpendicular diameters of all measurable lesions;
- (ii) absence of new lesions, and
- (iii) lack of progression of any preexisting lesions.

Claim 10 (*previously amended*): The method of claim 9 wherein said antitumor response further comprises the disappearance of all evidence of melanoma disease for at least one month.

Claim 11. (withdrawn) The method of claim 9, wherein said inhibitor is a MEK-directed protease.

Claim 12. (withdrawn). The method of claim 11, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

Claim 13 (*previously amended*): The method of claim 9 wherein said inhibitor is selected from the group consisting of PD98059, U0126 and PD184352.

Claim 14 (*previously amended*): The method of claim 13 wherein said inhibitor is PD184352.

Claim 15 (*previously amended*): The method of any of claims 9, 10, 13 or 14, wherein said mammal is a human.

Claim 16 (*currently amended*): A method of inhibiting growth or recurrent growth of a melanoma tumor in a mammal having melanoma or at risk for melanoma growth or recurrence, comprising administering an effective amount of an organic small molecule inhibitor of MEK enzyme to said mammal, said inhibitor being a direct, noncompetitive inhibitor of MEK that does not inhibit the binding of the enzyme to one of its substrates, ATP, thereby inducing a cytotoxic response leading to apoptosis of melanoma cells in said mammal, which response inhibits said growth or recurrent growth of said melanoma tumor.

Claim 17. (withdrawn) The method of claim 16 wherein said inhibitor is a MEK-directed protease.

Claim 18. (withdrawn) The method of claim 17, wherein said protease is *Bacillus anthracis* lethal factor or a functional derivative thereof.

Claim 19 (*previously amended*): The method of claim 16 wherein said inhibitor is selected from the group consisting of PD98059, U0126 and PD184352.

Claim 20 (*previously amended*): The method of claim 19 wherein said inhibitor is PD184352.

Claim 21 (*previously amended*): The method of any of claims 16, 19 or 20, wherein said mammal is a human.